CLAIMS

1. An engineered CHO cell, including an engineered CHO-K1, comprising:

a genome of the CHO cell, in which the genome comprises one or more alterations comprising:

deletions,

additions, and/or

substitutions,

of one or more nucleic acids in one or more, generally, more than 10, 20, 30, 40, 50, 60, 80, 90 or 100 endogenous retrovirus (ERV) elements which are part of the genome;

in which the CHO cell further comprises heterologous nucleic acid sequences encoding one or more sequences or proteins inhibiting one or more proteins of a recombination pathway, and/or heterologous nucleic acid sequences encoding one or more sequences or proteins suppressing expression of the one or more proteins of a recombination pathway, preferably HR (homologous recombination), even more preferably Nbs1, Mre11, Rad51, Ligase 1 and/or Ligase 3.

2. An engineered CHO cell according to Claim 1, in which the ERV elements are from gamma retroviral ERVs, including Koala epidemic viral (KoRV), Mouse Mammary Tumor Viral (MMTV), Mouse Leukemia Viral (MLV) ERVs and in which the one or more alterations are adapted to suppress or eliminate release of one or more, preferably more than 60%, 70%, 80%, 90%, 95% or 100% of the ERVs.

3. An engineered CHO cell according to Claim 1 or 2, in which the one or more (ERV) elements are or are from a *gag, pol* and/or *env* gene, preferably from the gag gene, encoding a MA (matrix), CA (capsid), NC (nucleocapsid), a further domain encoding proteins such as pp12 or p6 and/or are long terminal repeats (LTRs) of a ERV.

4. An engineered CHO cell according to Claim 3, in which the one or more ERV elements encode a Gag (groups antigen) protein, a Pol (reverse transcriptase) protein and/or an Env (envelope) protein.

5. An engineered CHO cell according to any preceding claim, in which the deletions, additions or substitutions comprise more than 2, 3, 4, 5, 10, 15, 20, 25, 30, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 150 or 200 nucleic acids; and/or

in which the alterations are additions in form of targeted integrations and the one or more (ERV) elements are or are from one or more *gag*, *pol* and/or *env* genes, preferably gag genes, and sequences of the *gene* were subjected to the targeted integrations of a transgene, preferably, encoding a marker protein such as GFP (green fluorescent protein), and/or when the alteration(s) result in a dominant-negative phenotype; and/or

in which the ERV elements are from a gag gene and at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95%, 98%, 99% or all of the elements comprise the alterations; and/or

in which the alterations are in consensus sequences of the ERV elements, in which the consensus sequence is at least 5, 10, 15, or 20 base pairs long, preferably between 15 and 25 or between 30 and 50 base pairs long; and/or

in which the engineered CHO cell releases no or substantially no ERVs.

6. An engineered CHO cell according to any preceding claim, in which the heterologous nucleic acid sequences are present as a vector that is not integrated into the genome of the CHO cell.

7. An engineered CHO cell according to any preceding claim, further comprising heterologous donor DNA, preferably on a vector, encoding one or more marker protein such as GFP (green fluorescent protein); and/or

in which the engineered CHO cell further comprises a transgene; and/or

in which the transgene is a marker gene encoding a marker protein such as GFP (green fluorescent protein) and/or a biotherapeutic which is preferably integrated into the genome; and/or

in which the engineered CHO cell comprises one or more of the ERV elements, such as a gag gene or a ERV element being from the gag gene, that comprises a PPYP motif and in which (i) sequences encoding the PPYP motif and/or sequences of up to 20 nucleic acids flanking the sequences in (i) comprise the alternation; and/or

in which the engineered CHO cell has deletions, additions, and/or substitutions in one or more SEQ IDs 1, 2, 3, 4 or sequences having more than 90% or 95% sequence identity therewith, preferably within the ERV elements of the sequences; and/or

in which the engineered CHO cell has deletions, additions, and/or substitution in ERV group 1 consensus sequence, such as SEQ ID NO. 30 or sequences having more than 90% sequence identify therewith and in which the sequence with the deletions, additions, and/or substitution does not encode a functional Gag protein; and/or

in which the one or more alterations are the substitution of one or more myristoylated amino acids within a myristoylation motif in one or more of the ERV elements, such as a gag gene or an ERV element being from the gag gene, with a non-myristoylated amino acid, in which the engineered CHO cell comprises, at least transiently:

sequences, such as in form of a transiently expressed vector encoding HR and/or MMEJ proteins such as Pad51, Lig3, Ercc1, Pold3; and/or

sequences, such as siRNA sequences, such as siMRe11 or vectors encoding the same.

8. A method for producing an engineered CHO cell according to any preceding claim, the method comprising:

(i) introducing a heterologous system for introducing single or double stranded breaks into a target nucleic acid sequence, such as a consensus sequence of an ERV element, preferably an ERV element that is or is from a *gag* gene into a CHO cell, and further

(ii) introducing into the CHO cell,

(a) heterologous nucleic acid sequences encoding one or more sequences or proteins inhibiting one or more proteins of one or more of the recombination pathways, and/or

(b) heterologous sequences encoding one or more sequences, such as siRNAs, or proteins suppressing expression of the one or more proteins of one or more of the recombination pathways,

in which the heterologous system of (i) and/or sequences of (ii)(a) and/or (ii)(b) are preferably at least transiently expressed in the CHO cell.

9. A method according to Claim 8, in which the heterologous sequences encode one or more sequences or proteins inhibiting one or more or proteins of a recombination pathway, in

particular one or more proteins of Homologous Recombination (HR), in particular Rad51; and/or

in which a marker gene, such as GFP, is inserted into the target nucleic acid sequence via homologous recombination and in which cells comprising the marker gene are preferably selected; and/or

in which the heterologous nucleic acid sequences of (a) encode or activate proteins of the MRN complex, such as Nbs1 and/or Mre 11, and/or in which the heterologous sequences of (b) encode sequences or proteins suppressing expression of one or more proteins of the HR pathway such as Rad51; and/or

in which a deletion or insertion is introduced into the one or more ERV elements via non-homologous end-joining (NHEJ) or microhomology mediated end joining (MMEJ); and/or

in which the heterologous sequences are part of integrating or non-integrating vectors;

and/or

in which the non-naturally occurring system for introducing single or double stranded breaks into a target nucleic acid sequence is a CRISPR/Cas9 system or is based thereon; and/or

in which one or more myristoylated amino acids within a myristoylation motif in one or more of the ERV elements is substituted with a non-myristoylated amino acid, the method being preferably performed during the transient expression of sequences encoding HR and/or MMEJ proteins such as Pad51, Lig3, Ercc1, Pold3; and/or sequences, such as siRNA sequences, such as siMRe11 or vectors encoding the same; and/or

in which the cell comprises one or more of the ERV elements, a PPYP motif and in which (i) sequences encoding the PPYP motif and/or sequences of up to 20 nucleic acids flanking the sequences in (i) comprise an alteration, the method being preferably performed during the transient expression of RNA sequences suppressing expression of HR proteins such as Rad51.

10. An engineered CHO cell, including a CHO-K1, and in which a genome of the cell comprises one or more alterations comprising:

(a) deletions,

(b) additions, and/or

(c) substitutions,

of one or more nucleic acids in one or more, generally, more than 10, 20, 30, 40, 50, 60, 80, 90 or 100 endogenous retrovirus (ERV) elements, and is produced by a method according to Claim 9 or 10.